PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF TRANSMITTAL
OF COPIES OF TRANSLATION
OF THE INTERNATIONAL PRELIMINARY REPORT
ON PATENTABILITY
(CHAPTER I OR CHAPTER II
OF THE PATENT COOPERATION TREATY)
(PCT Rules 44*bis*.3(c) and 72.2)

To:

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受付
18.7.14
岩谷国際特許
事務所

Date of mailing *(day/month/year)* 06 July 2006 (06.07.2006)	
Applicant's or agent's file reference K12F1391	**IMPORTANT NOTIFICATION**
International application No. PCT/JP2004/011696	International filing date *(day/month/year)* 13 August 2004 (13.08.2004)
Applicant TAKEO, Satoshi et al	

1. **Transmittal of the translation to the applicant.**

☑ The International Bureau transmits herewith a copy of the English translation of the international preliminary report on patentability (Chapter I).

☐ The International Bureau transmits herewith a copy of the English translation of the international preliminary report on patentability (Chapter II).

2. **Transmittal of the copy of the translation to the designated or elected Offices.**

The International Bureau notifies the applicant that copies of that translation have been transmitted to the following designated or elected Offices requiring such translation:

None

The following designated or elected Offices, having waived the requirement for such a transmittal at this time, will receive copies of that translation from the International Bureau only upon their request:

AE, AG, AL, AM, AP, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EA, EC, EE, EG, EP, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OA, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

3. **Reminder regarding translation into (one of) the official language(s) of the elected Office(s).**

The applicant is reminded that, where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary report on patentability (Chapter II).

It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned within the applicable time limit (Rule 74.1). See Volume II of the PCT Applicant's Guide for further details.

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer Masashi Honda
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PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY
(Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44*bis*)

Applicant's or agent's file reference K12F1391	**FOR FURTHER ACTION**	See item 4 below
International application No. PCT/JP2004/011696	International filing date *(day/month/year)* 13 August 2004 (13.08.2004)	Priority date *(day/month/year)* 14 October 2003 (14.10.2003)
International Patent Classification (8th edition unless older edition indicated) See relevant information in Form PCT/ISA/237		
Applicant TAKEO, Satoshi		

1. This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 *bis*.1(a).

2. This REPORT consists of a total of 7 sheets, including this cover sheet.

   In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.

3. This report contains indications relating to the following items:

☒	Box No. I	Basis of the report
☐	Box No. II	Priority
☒	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☒	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☐	Box No. VIII	Certain observations on the international application

4. The International Bureau will communicate this report to designated Offices in accordance with Rules 44*bis*.3(c) and 93*bis*.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44*bis* .2).

	Date of issuance of this report 26 June 2006 (26.06.2006)
The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No. +41 22 338 82 70	Authorized officer Masashi Honda e-mail: pt08@wipo.int

Form PCT/IB/373 (January 2004)

PATENT COOPERATION TREATY

TRANSLATION

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

	Date of mailing *(day/month/year)*
Applicant's or agent's file reference K12F1391	FOR FURTHER ACTION See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/JP2004/011696	13.08.2004	14.10.2003

International Patent Classification (IPC) or both national classification and IPC

Applicant
TAKEO, Satoshi

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☒ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/JP	Authorized officer
Facsimile No.	Telephone No.

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/JP2004/011696

Box No. I Basis of this opinion

1. With regard to the language, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This opinion has been established on the basis of a translation from the original language into the following language _____, which is the language of a translation furnished for the purposes of international search (under Rule 12.3 and 23.1(b)).

2. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

a. type of material

☐ a sequence listing

☐ table(s) related to the sequence listing

b. format of material

☐ in written format

☐ in computer readable form

c. time of filing/furnishing

☐ contained in the international application as filed.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/JP2004/011696

Box No. III **Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application

☒ claims Nos. 13-18

because:

☒ the said international application, or the said claims Nos. 13-18
relate to the following subject matter which does not require an international preliminary examination (*specify*):

The subject matters of claims 13-18 are methods for treatment of the human body by therapy. (PCT Article 34(4)(a)(i) and PCT Rule 67.1(iv))

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. _____
are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. _____ are so inadequately supported
by the description that no meaningful opinion could be formed.

☒ no international search report has been established for said claims Nos. 13-18

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form
- ☐ has not been furnished
- ☐ does not comply with the standard

the computer readable form
- ☐ has not been furnished
- ☐ does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See Supplemental Box for further details.

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/JP2004/011696

Box No. IV Lack of unity of invention

1. ☒ In response to the invitation (Form PCT/ISA/206) to pay additional fees the applicant has:

   ☒ paid additional fees

   ☐ paid additional fees under protest

   ☐ not paid additional fees

2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

   ☐ complied with

   ☒ not complied with for the following reasons:

Claims 1-12 and 19-24

It is considered that the technical feature common to claims 1-12 and 19-24 is a pharmaceutical product having a hepatocyte growth factor as an active ingredient.

However, a pharmaceutical product having a hepatocyte growth factor as an active ingredient has been publicly known (see the documents cited in "Notification of Results of Partial International Search" in the attached document, if necessary), and so only with the above-mentioned technical feature, there is no technical relationship in the inventions of the present application involving one or more of the same or corresponding special technical features. Therefore, the present application does not relate to a single invention, nor a group of inventions so linked as to form a single general inventive concept, and so does not satisfy the requirement of unity of invention.

Finally the present application contains two different inventions based on the technical features of combinations of a hepatocyte growth factor as an active ingredient with specific diseases to be treated with it, the said inventions not meeting the requirement of unity of invention.

i) The invention of claims 1-4, 7-10 and 19-22
ii) The invention of claims 5, 6, 11, 12, 23 and 24

4. Consequently, this opinion has been established in respect of the following parts of the international application:

   ☐ all parts

   ☒ the parts relating to claims Nos. 1-12, 19-24

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/JP2004/011696

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	6, 12, 24	YES
	Claims	1-5, 7-11, 19-23	NO
Inventive step (IS)	Claims		YES
	Claims	1-12, 19-24	NO
Industrial applicability (IA)	Claims	1-12, 19-24	YES
	Claims		NO

2. Citations and explanations:

This opinion is based on the descriptions in the following documents cited in the ISR:
Document 1: WO, 95-07709, A1 (Sumitomo Pharmaceuticals Co., Ltd.)
Document 2: JP, 7-41429, A (Mitsubishi Chemical Corp.)
Document 3: WO, 01-21214, A1 (MedGene Bioscience Co., Ltd.)
Document 4: Society for Neuroscience Abstracts, (M. Akimoto, et al.), 1998, 24(1-2), page 687
Document 5: Society for Neuroscience Abstracts, (N. Matsuki, et al.), 2000, 26(1-2), Abstract no. 420.1
Document 6: (Maki Yamada, et al.), Proceedings of the 24th Annual Meeting of the Neuroscience Society 2001, page 392
Document 7: (S. Takeo, et al.), Biochemistry, 2003, 75(8), abstract no. 4S81-5, page 774
Document 8: WO, 03-037365, A1 (The Johns Hopkins University)
Document 9: (Koran Ryu, et al.), J. Jpn. Med. Soc. Biol. Interface, 2000, 31, pages 11-16
Document 10: WO, 02-30908, A1 (Knoll GmbH)
Document 11: JP, 2003-506368, A (BASF AG.)

Claims 1-4, 7-10 and 19-22

Document 1 (the claims, examples, page 8, lines 18-28, and page 9, lines 25-30) mentions that HGF is useful for the treatment of nerve degeneration illness such as dementia and Alzheimer disease. Document 2 (the claims, examples and paragraph [0015]) mentions that HGF is useful for the treatment of dementia including Alzheimer's disease, memory disorder, neural disorder, and so on. Document 3 (the claims and examples) mentions that HGF is useful for the treatment or prevention of cerebrovascular diseases, specifically including brain infarction and Alzheimer's dementia. Documents 4 and 5 mention that HGF is useful for improving learning difficulty. Document 6 mentions that HGF is useful for the acquisition and fixing of memory. Document 7 mentions that HGF improves long memory retention dysfunction, and is useful for the improvement of higher central dysfunction.

Accordingly, the subject matters of claims 1-4, 7-10 and 19-22 are described in documents 1-7.

Accordingly, the subject matters of claims 1-4, 7-10 and 19-22 do not appear to be novel or to involve an inventive step in view of the descriptions in documents 1-7.

Claims 5, 6, 11, 12, 23 and 24

Document 8 (the claims and examples) and document 9 mention that HGF inhibits vascular hyperpermeability, particularly in pulmonary disorders.

The subject matters of claims 6, 11 and 24 are different from the inventions of documents 8 and 9 in that the said subjects are restricted to cases where the blood vessels are brain blood vessels; however, it is publicly known, as mentioned in documents 10 and 11, that diseases due to vascular

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

hyperpermeability can occur in pulmonary as well as in brain blood vessels, and pharmaceutical products for vascular hyperpermeability are often useful for both pulmonary and brain blood vessels. Accordingly, using HGF described in documents 8 and 9 for improving vascular hyperpermeability in brain blood vessels would not have required particular creativity for a person skilled in the art.

So, the subject matters of claims 5, 11 and 23 do not appear to be novel or to involve an inventive step in view of the descriptions in documents 8 and 9, and the subject matters of claims 6, 12 and 24 do not appear to involve an inventive step in view of the descriptions in documents 8-11.